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Meta-Analysis of DNA Methylation and Expression in Liver Cancer Patients

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ABSTRACT

Hepatocellular carcinoma (HCC), the most common liver cancer, is the second leading cause of cancer-related death worldwide. HCC is often diagnosed at late stages, for which there are no effective chemotherapies. Biomarkers unique to HCC patients could be used to detect HCC early and improve treatment. In the present project, we have performed a meta-analysis to compare the gene-specific DNA methylation and gene expression patterns of HCC patients as reported by four independent studies. Our goal was to discover the strongest changes that distinguish HCC from normal tissue. The relationship between methylation and expression in HCC was examined and genes epigenetically regulated in HCC were identified. The top changes within genes, gene families and pathways could be of interest in further investigations of potential HCC biomarkers. A significant correlation between DNA hypomethylation and gene activation and between DNA hypermethylation and gene silencing was found. CpG islands, commonly found in promoter regions, are predominantly hypermethylated in HCC, while CpGs outside of CpG islands are predominantly hypomethylated in gene bodies. 149 genes were found to be significantly differentially methylated between tumors and normal adjacent tissue, and 169 genes were found to be significantly differentially expressed. Genes identified for further research are GNG7, WNT5B, RXRG, HOXB7, and SMARCB1. No overlap was found between differentially expressed and methylated genes. Nevertheless, common gene families and pathways were identified where more potential biomarkers could be found in future studies.

KEYWORDS

HCC, liver cancer, meta-analysis, biomarkers, epigenetics, methylome, transcriptome, DNA methylation, patients,